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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,178	07/08/2003	Dennis M. Brown	A-71462/RFT/THR (468899-3)	1122
32940 7590 12/29/2006 DORSEY & WHITNEY LLP 555 CALIFORNIA STREET, SUITE 1000 SUITE 1000 SAN FRANCISCO, CA 94104			EXAMINER DESAI, RITA J	
			ART UNIT	PAPER NUMBER
			1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/29/2006	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/616,178

Applicant(s)

BROWN, DENNIS M.

Examiner

Rita J. Desai

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-7 and 15-28 is/are pending in the application.
- 4a) Of the above claim(s) 3,4 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 5-7, 15-22 and 24-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/16/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

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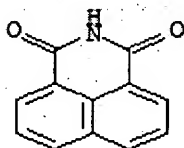
### DETAILED ACTION

The examiner had done a New Restriction in paper mailed 6/14/06.

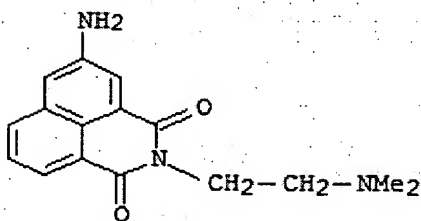
The applicants elected the group with claims 5-7, 15-22 and 24-28 without traverse and claims 3-4 and 23 were withdrawn.

The examiner had initially rejected claims 5-7, 15-22 in the paper mailed 15/04 and also 10/24/05 .

It should be noted that Applicants specifications are interchanging using amonafide and naphthalimide.



Naphthalimide is given by the structure and amonafide is



Applicants 's examples and definition of the naphthalimide as given in the specifications includes amonafide as applicants naphthalimide comprises atleast 2 amine groups.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 15-22, 24-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the Written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that applicant were in possession of the claimed invention. Applicant's claims are drawn to "naphthalimide salts comprising at least two amine groups" The specification defines in figure 1 the amonafide . There is no structure given to the other naphthalimide salts. The specification gives no guidance to one of ordinary skill in the art the attachment position or type of other group to form other analogs. The specification does not define the compound in this category. The analogs would includes a plethora of compounds, which has this core.

The expression *naphthalimide salts comprising at least two amine groups* with out any structure and just a mere recitation of the term does not convey to one of ordinary skill in the art that applicants were in possession of the claimed subject matter. The language recited without any correlation does not meet the written description requirement for the expression "*naphthalimide salts comprising at least two amine groups* " as one of ordinary skill in the art could not recognize or understand the structure from it . Claims employing language at the point of novelty, such as applicants', neither provide those elements required to practice the inventions, nor "inform the public" during the life of the patent of the limits of the monopoly

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asserted. The expression could encompass myriad of compounds and applicants claimed expression represents only an invitation to experiment regarding possible compounds.

### *Claim Rejections - 35 USC § 102*


The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7, 15-22, 24-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Brana et al US 5420137.

Brana'137 discloses the injectable solutions see example E in column 3 of the reference.

Example E		
Preparation of amonafide injection concentrate as lyophilisate		
	Amonafide 2HCl	3.992 kg
	NaOH, 5 m	1.994 kg
	Water for injection ad	20.000 kg
The solution was sterilized by filtration and subsequently dispensed in 2 ml portions into vials of glass type I (brown glass) and freeze-dried. The pH of the reconstituted solution was $5.5 \pm 0.5$ , the osmolarity was		

The reference discloses the amonafide 2HCl, which is at least 1.5 mole equivalent of the two amine groups are protonated.

It uses water for the injection and the pH of the solution is  $5.5 \pm 0.5$  which comes to about 6.

The limitations of claims 15-22, 24-28, are clearly met.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

- Claims 5-7, 15-22, 24-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brana et al US 5420137 and Brana et al II ( US 5, 552, 544).

Applicants claims are drawn to a process of making the naphthimide salts and aqueous solution consisting essentially of naphthalimide

Determination of the scope and content of the prior art (MPEP §2141.01)

The prior art teaches several process of making the monohydrochloride salt of amonafide.

See the whole document. It also teaches using a calculated amount of the acid to make the monohydrochloride salt.

Example D in column 2 teaches the inject able solution at 56.2mg/ml concentration which is within the scope of claim 15 and 17.

The limitation of claim 22 “adding a base to said aqueous solution” to form a naphthalimide salt is also met. See example E, column 3.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

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The prior art does not specifically give the amount to make the dihydrochloride salt, nor does it mention the other salts as given in claim 7.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

One of skill in the art would have been motivated to make the di-hydrochloride salt, or other pharmaceutically acceptable salts such as those given in claim 7, as the compound has 2 amine groups, and using the appropriate mole equivalent would give the corresponding salt with at least 1.5 mole equivalent of the said amine are protonated. The aqueous solutions suitable for administration by injection are also taught.

Thus, it would be prima facie obvious to modify the teachings of Brana et al and Brana et al I by reacting the naphthalimide with an acid to make the monoammonium salt first, and then with the excess acid to make a diammonium salt from the monoammonium salt using the teachings of Brana et al II. It is also obvious that acid is reactive to amino group, thus, the acid would react with all the amino group(s) available of the naphthalimide; i.e., monoammonium salt and diammonium salt will be formed in the reaction medium at a different ratio. Thus, the claimed invention would be deemed obvious over the prior art teachings in the absence of unexpected and/or unobvious results.

- The above rejection further in view of US 6693198 (102(e) date) for claims 6 and 7.

US 6693198 teaches the different salts such as the maleate, glycolates and so on.

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Thus in view of US '198 Ajami et al, Brana et al '137 can be modified to include the different salts of naphthalimide. See the claims of US '198.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 23-25, 60-63 of copending Application No. 10/976,961. Although the conflicting claims are not identical, they are not patentably distinct from each other because the co-pending application has claims drawn to a composition and the applicants claims are drawn to an aqueous solution for administration in the injectable form of the same compound, which would constitute a composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.



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Claims 15-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11 and 12 of copending Application No. 11/048614. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the co-pending application is also drawn to a composition of the same compound.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai  
Primary Examiner  
Art Unit 1625

*R. Desai*  
12/18/06

R.D.  
December 18, 2006